Discovering Cellular Respiration: Background Reading

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Review of Aerobic Cellular Respiration

Cellular respiration consists of several processes that function together to convert nutrient molecules (macromolecules) into usable energy (ATP, adenosine triphosphate) to fuel cellular functions. The process of cellular respiration is analogous to a car assembly line running in reverse. Energy substrates like glucose, fatty acids and amino acids are sequentially broken down (disassembled). Energy is released during the break down and captured by converting ADP (adenosine diphosphate) into ATP. For simplicity, cellular respiration is often taught in the context of glucose break down because all four of the major processes that make up cellular respiration are utilized (Figure 1). Further, the outputs (products) of one process are often the inputs (substrates) for another process. For example, the acetyl-CoA produced during pyruvate processing is a major input for the citric acid cycle. Below is a brief description of the four processes involved in the breakdown of glucose (refer to Figure 1).

1. ***Glycolysis*** – The purpose of this ten-step process is to rearrange and convert glucose (6 carbons) into two separate molecules of pyruvate (3 carbons). Initially, energy (ATP) is invested into this process. Later, energy is released and captured by 1) converting ADP to ATP using substrate-level phosphorylation and 2) in the form of high-energy electrons that reduce the coenzyme NAD^+ to NADH.
2. ***Pyruvate Processing*** – The purpose of this process is to convert pyruvate into an acetyl group and link it to Coenzyme A (CoA). Also, high-energy electrons are harvested by NAD^+ which is converted to NADH.
3. ***Citric Acid Cycle*** **(CAC)** – The purpose of this process is to harvest the remaining energy stored in the two-carbon acetyl group (remember it started as 6 carbons). The CAC produces one ATP and captures 8 high-energy electrons with NAD^+ and FAD^+, which converts them to NADH and $FADH_2$, per acetyl-CoA.
4. ***Electron Transport Chain*** **(ETC)** – The purpose of this process is to transfer the energy stored in high-energy electrons into usable energy by producing ATP. This step utilizes O_2 as the terminal electron acceptor and chemiosmosis is used to generate ATP by oxidative phosphorylation. In addition, this step is critical for regenerating NAD^+ and FAD^+.

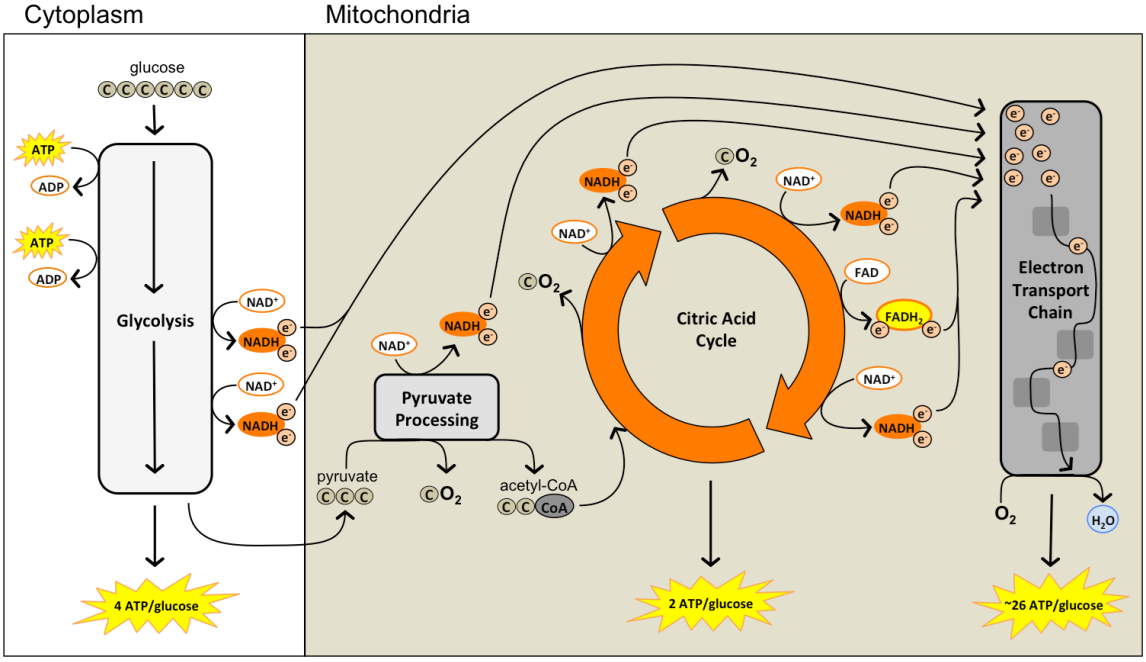

Figure 1 Overview of Cellular Respiration in Eukaryotes
This diagram allows you to trace the carbon atoms that were part of glucose being released as CO2, and the electrons that originate in glucose being used to generate ATP in the electron transport chain.

Fermentation

In the absence of oxygen (anaerobic conditions) or in an oxygen-deprived state (during an intense workout), the pyruvate produced by glycolysis remains in the cytoplasm where it is reduced (gains electrons). In animals, an enzyme called lactate dehydrogenase transfers electrons from NADH to pyruvate to produce lactate (lactic acid) and NAD^+ (Figure 2). The purpose of this process is to regenerate NAD^+ to be used again during glycolysis. Without fermentation, glycolysis would stop because all of the NAD^+ would remain reduced as NADH.

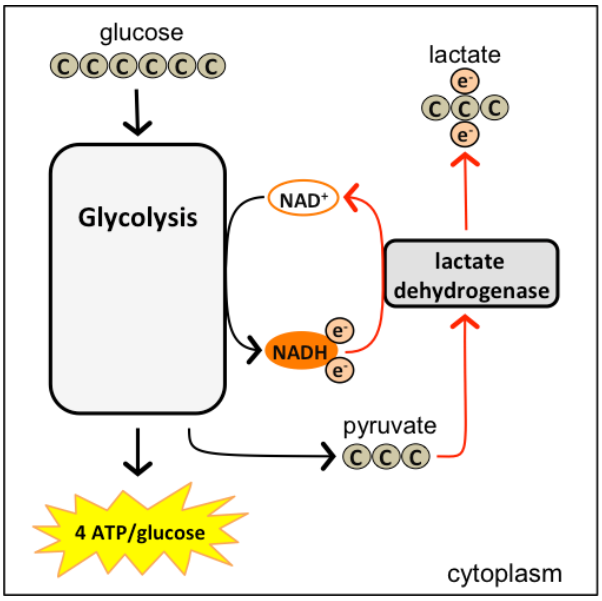

Figure 2 Lactic Acid Fermentation

Regulation of Cellular Respiration

The mechanisms regulating cellular respiration are elaborate. They ensure a sufficient supply of ATP and avoid the wasteful overproduction of ATP when supplies are high through *feedback inhibition* (negative feedback loops). Feedback inhibition occurs when a particular intermediate (or output) inhibits or slows down its own production when its concentration is at a sufficient level (Figure 3). Many of the metabolic intermediates of cellular respiration regulate their own production in this manner.

Figure 4 represents a simplified view of where feedback inhibition occurs in cellular respiration and shows that the outputs of each process (i.e., pyruvate, acetyl-CoA, NADH and $FADH_2$) can inhibit or slow down their own production. For example, if the electron transport chain was damaged or inhibited NAD^+ and FAD^+ could no longer be regenerated resulting in the build-up of NADH and $FADH_2$. As the levels of NADH and $FADH_2$ increase in the mitochondria, they will begin to inhibit both pyruvate processing and citric acid cycle. As the citric acid cycle slows down, acetyl-CoA levels will rise which will further inhibit pyruvate processing. Interestingly, glycolysis could continue in this situation because an alternative pathway, lactic acid fermentation, allows for pyruvate and NADH to be processed within the cytoplasm preventing them from building up and inhibiting their own production.

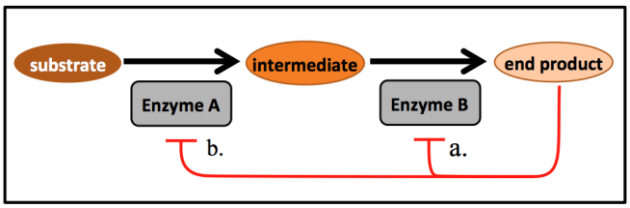

Figure 3 Feedback Inhibition
A simple metabolic pathway that requires two enzymes and contains one intermediate metabolite. (a) The end product inhibits its own production directly. (b) The end product inhibits its own production indirectly by inhibiting an upstream enzyme.

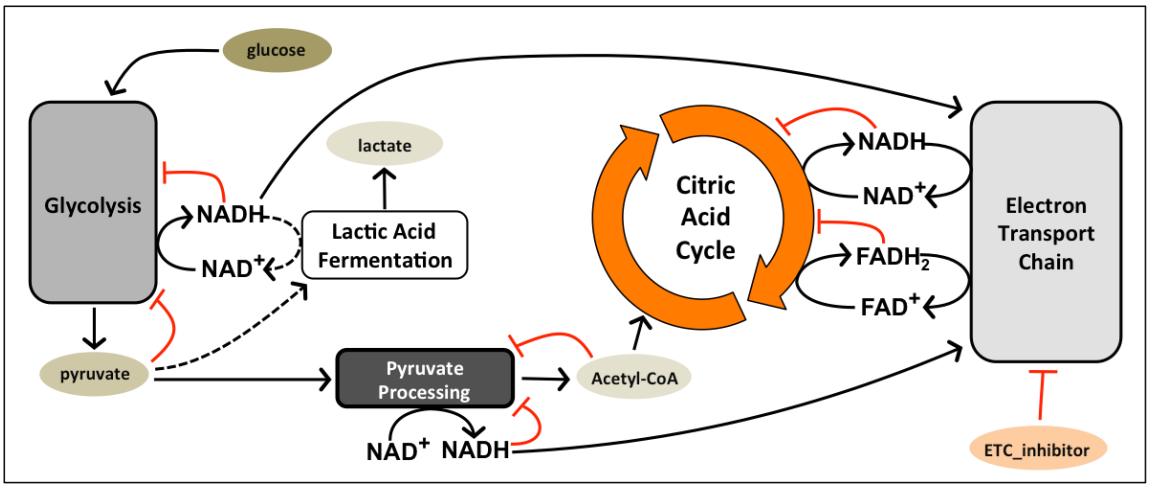

Figure 4 Regulation of Cellular Respiration

Investigating Cellular Respiration with a Computational Model and Simulations

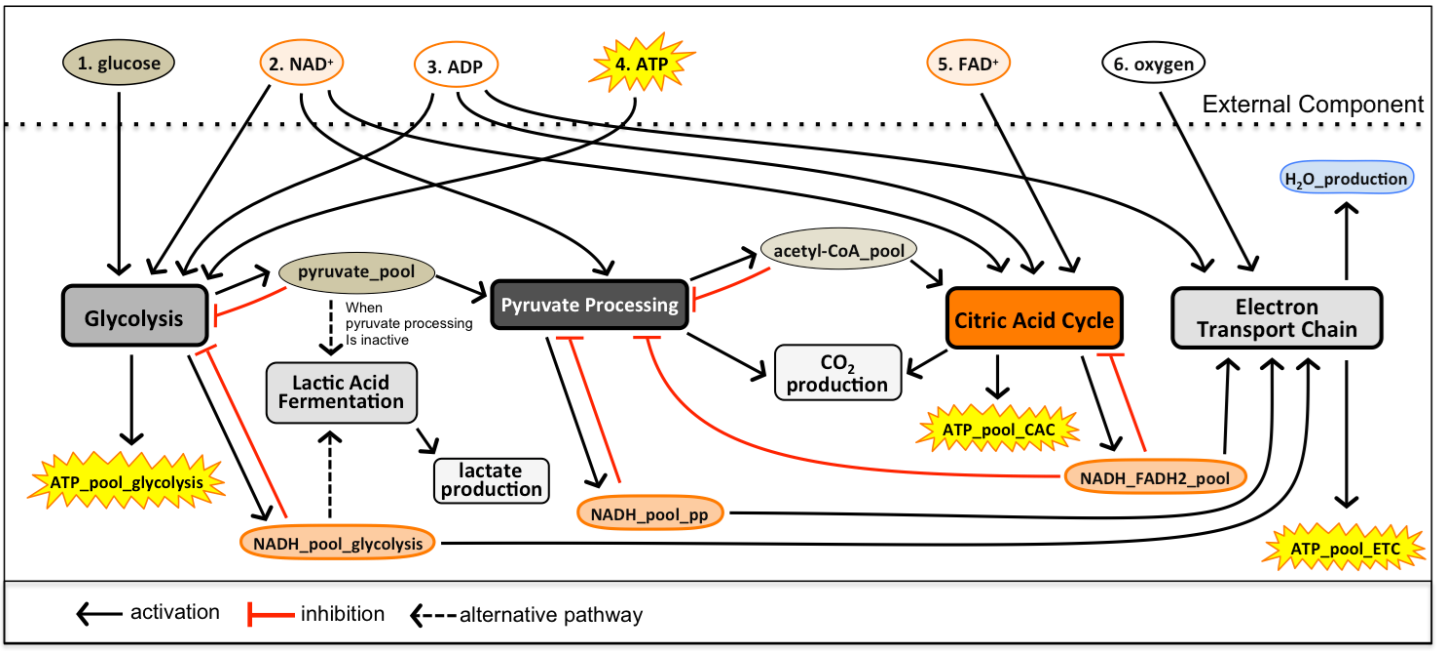

Figure 5 Cellular Respiration Dynamic Model

Computational Model of Cellular Respiration

In this activity you will be using a computational modeling and simulation software called the Cell Collective to explore the components and dynamics of cellular respiration. Figure 5 represents a simplified computational model of cellular respiration that was built using the Cell Collective. The components of the model represent important molecules (e.g., glucose and ADP) and processes (e.g., glycolysis and pyruvate processing). The components are connected using arrows to represent positive regulation (activation) and blunted lines to represent negative regulation (inhibition) which are collectively called *interactions*. Simulating the model allows you to observe all of the components interacting together and mimics the activities occurring in a cell. To interpret simulation data, it is critical that you understand the model components and their functions.